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TITLE: Compositions and methods for diagnosis and treatment of cardiovascular disorders

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US-CL-CURRENT: 424/85.1

CLAIMS:

1. A method of upregulating a cytokine profile characteristic of a Th1 T-cell response relative to a cytokine profile of a Th-2 T-cell response associated with inflammation of blood vessels in a cardiovascular disorder, comprising administering to a subject in need thereof an effective amount of one or more probiotic agents for prophylaxis or treatment of the inflammation.

2. A method according to claim 1 wherein the method is a method of treating the inflammation.

3. A method according to claim 1 comprising shifting the cytokine profile characteristic of a Th2 T-cell response to a cytokine profile characteristic of a Th1 response.

4. A method according to claim 1 comprising administering a probiotic agent capable of upregulating a Th1 T-cell response and suppressing a Th2 T-cell response in the subject.

5. A method according to claim 1 comprising administering a probiotic agent capable of potentiating the action of cytokines characteristic of a Th1 T-cell response and suppressing the action of cytokines characteristic of a Th2 response in the subject.

6. A method according to claim 1 comprising administering a probiotic agent capable of upregulating a Th1 T-cell response in the subject.

7. A method according to claim 1 comprising administering a probiotic agent capable of potentiating the action of cytokines characteristic of a Th1 T-cell response in the subject.

8. A method according to claim 1 comprising administering a probiotic agent capable of suppressing a Th2 T-cell response in the subject.

9. A method according to claim 1 comprising administering a probiotic agent capable of suppressing the action of cytokines characteristic of a Th2 T-cell response in the subject.

10. A method according to claim 1 wherein the one or more probiotic agents comprises a microorganism, extract or sonicate, or a mixture of some or all of the foregoing.

11. A method according to claim 10 wherein the extract comprises a cell wall fraction of the microorganism.

12. A method according to claim 11 wherein the microorganism is selected from the group consisting of yeast and bacteria.

13. A method according to claim 12 wherein the microorganism is a probiotic bacterium.

14. A method according to claim 13 wherein the probiotic bacterium is selected from the group consisting of Lactobacillus and Mycobacterium species.

15. A method according to claim 14 wherein the Lactobacillus species is capable of suppressing a Th2 response and lowering cholesterol level in the subject.

16. A method according to claim 13 wherein the probiotic bacterium is selected from Lactobacillus acidophilus, Lactobacillus fermentum, and Mycobacterium vaccae.

17. A method according to claim 12 wherein the microorganism is a bacterium selected from the group consisting of Lactobacillus casei, Lactobacillus plantarum, Lactobacillus chamnosus and Bifidobacterium breve.

18. A method according to claim 10 wherein the microorganism is viable.

19. A method according to claim 1 or 2 further comprising administering to the subject an effective amount of at least one pharmaceutically active agent for treating the subject in addition to the probiotic agent for up regulating a cytokine profile characteristic of a Th1 T-cell response.

20. A method according- to claim 19 wherein the pharmaceutically active agent is selected from the group consisting of lipid-lowering drugs, anti-hypertensive agents and anti-diabetic agents.

21. A method according to claim 19 wherein the probiotic agent for up regulating the cytokine profile characteristic of the Th1 T-cell response is administered to the subject prior to, simultaneously with or subsequent to at least one pharmaceutically active agent.

22. A method according to claim 1 wherein the Th2 T-cell response associated with the disorder is exacerbated by bacterial infection, bacterial antigens, polyclonal activators, superantigens or autoantigens.

23. A method according to claim 22 wherein the infection is by, or the bacterial antigen is from, Chlamydia pneumoniae, Helicobacter pylori or non-typable Haemophilus influenzae.

24. A method according to claim 1 or 2 wherein the cardiovascular disorder is selected from stable or unstable clinical cardiovascular disease, degenerative vascular disease, atheroma and coronary artery disease.

25. A method according to claim 2-4 wherein the cardiovascular disorder is selected from the group consisting of subjects suffering from atheroma with stable or unstable clinical disease.

26. A method of diagnosing or evaluating susceptibility to inflammation of blood vessels associated with a cardiovascular disorder, comprising evaluating a T-cell response in a subject wherein an upregulated Th2 T-cell response and/or suppressed Th1 T-cell response is indicative of susceptibility to, or the presence of, the disorder.

27. A method according to claim 26 comprising determining whether the subject has an upregulated Th2 T-cell response and a suppressed Th1 T-cell response.

28. A method according to claim 26 wherein the evaluating comprises determining whether the activity or production of one or more cytokines characteristic of the Th1 T-cell response is suppressed and/or whether the activity or production of one or more cytokines characteristic of a Th2 T-cell response is potentiated.

29. A method according to claim 28 wherein the evaluating comprises determining whether the activity or production of one or more cytokines characteristic of Th1 T-cell response is suppressed and whether the activity or production or one or more cytokines characteristic of a Th2 T-cells response is potentiated.

30. A method according to claim 28 or 29 wherein the cytokine or cytokines are selected from the group consisting of IFN-.gamma., IL-4, IL-10 and IL-12.

31. A method according to any one of claims 26 to 30 wherein the T-cell response is evaluated by analysis of circulating T-cells.

32. A method of diagnosing a cardiovascular disorder associated with inflammation of blood vessels or evaluating whether a subject is susceptible to the inflammation, comprising: (a) measuring one or more immunoglobulin levels affected by the disorder to obtain test data; and (b) comparing the test data with reference data to evaluate whether the subject is susceptible to, or has, the inflammation, wherein the one or more immunoglobulin levels are selected from the group consisting of total immunoglobulin isotype levels and levels of total immunoglobulin isotype subclasses.

33. A method according to claim 32 comprising measuring one or more IgG levels.

34. A method according to claim 33 comprising measuring total IgG2 subclass immunoglobulin.

35. A method according to claim 33 comprising measuring the level of an IgG2 subclass specific antibody.

36. A method according to claim 33 wherein a ratio of total IgG2 subclass to IgG2 subclass specific antibody, or an altered ratio of total IgG2 subclass to IgG2 subclass specific antibody, is indicative of susceptibility to, or presence of the disorder.

37. A method according to claim 32 wherein the cardiovascular disorder is selected from subjects suffering from stable or unstable clinical cardiovascular disease,

degenerative vascular disease, coronary artery disease and atheroma.

38. A kit when used in a method of diagnosing a cardiovascular disorder or evaluating whether a subject is susceptible to the disorder, wherein the method involves measuring one or more immunoglobulin levels effected by the disorder to obtain test data, and comparing the test data with reference data to evaluate whether the subject is susceptible to, or has, the cardiovascular disorder, and wherein the kit comprises one or more reagents for performing the method together with instructions for use, and the one or more immunoglobulin levels are selected from the group consisting of total immunoglobulin isotypes and levels of total immunoglobulin isotype subclasses.

39. A kit according to claim 37 wherein the one or more reagents are selected from antibodies, buffers and control reagents.

40. A kit when used in a method of diagnosing or evaluating susceptibility to a cardiovascular disorder, wherein the method involves evaluating a T-cell response in a subject wherein an unregulated TL2 T-cell response and/or suppressed the T-cell response is indicative of susceptibility to, or the presence of, the disorder and the kit comprises one or more reagents for performing the method together with instructions for use.

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(54) **COMPOSITION AND METHODS AFOR DIAGNOSIS AND TREATMENT OF CARDIOVASCULAR DISORDERS**

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(57) **ABSTRACT**

The present invention relates to methods for diagnosis, prevention and treatment of cardiovascular disorders or associated disorders and, in particular, to the use in such methods of regulating cytokine levels or activity. Compositions and kits suitable for use in the methods are described.

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CLAIMS:

1. A method of prophylactic or therapeutic treatment of a cardiovascular disorder or an associated disorder comprising administering to a subject in need thereof an effective amount of an agent capable of regulating a cytokine associated with the disorder in the subject.

2. A method according to claim 1 wherein the cytokine is selected from the group consisting of: interferon-.gamma. (INF-.gamma.), interleukin-4 (IL-4), interleukin-10 (IL-10) interleukin-12 (IL-12), interleukin-13 (IL-13) and TGF-.beta..

3. A method according to claim 1 wherein regulation of the cytokine is achieved by increasing or decreasing the level of the cytokine and/or by potentiating or inhibiting the activity of the cytokine.

4. A method according to claim 3 wherein the regulation of the cytokine is part of a more general switch from a Th2 to a Th1 cytokine profile.

5. A method according to claim 1 wherein the agent is a microorganism, or components, extract or secreted products of a microorganism.

6. A method according to claim 5 wherein the microorganism is yeast or bacteria.

7. A method according to claim 6 wherein the bacteria are probiotic bacteria.

8. A method according to claim 7 wherein the probiotic bacteria are selected from the following: Lactobacillus spp, Mycobacterium spp and Bifidbacterium.

9. A method according to claim 8 wherein the probiotic bacteria are Lactobacillus acidophilus or Mycobacterium vaccae.

10. A method according to claim 5 wherein the microorganism is alive.

11. A method according to claim 1 wherein the agent is an antibody or binding fragment thereof.

12. A method according to claim 11 wherein the antibody or binding fragment thereof is an anti-CD40 antibody or a binding fragment thereof.

13. A method according to claim 13 further comprising administration of one or more pharmaceutically active agents used to treat underlying conditions that may exacerbate the cardiovascular disorder.

14. A method according to claim 13 wherein the pharmaceutically active agent is selected from the following: a lipid-lowering drug, an anti-hypertensive agent and an anti-diabetic agent.

15. A method according to claim 13 wherein the agent used to regulate the cytokine level or activity is administered prior to, simultaneously with or subsequent to the one or more such pharmaceutically active agents.

16. A method according to claim 1 wherein the cardiovascular disorder or associated disorder is exacerbated by bacterial infection, bacterial antigens, polyclonal activators, super antigens or autoantigens.

17. A method according to claim 16 wherein the cardiovascular disorder or associated disorder is exacerbated by bacterial antigen from Chlamydia pneumoniae, Helicobacter pylori or non-typable Haemophilus influenzae.

18. A method of diagnosing, or evaluating susceptibility of a subject to, a cardiovascular disorder or associated disorder comprising detecting the level and/or activity of a cytokine associated with the disorder in the subject.

19. A method according to claim 18 wherein the level and/or activity of the cytokine is detected by analysis of circulating T-cells.

20. A method according to claim 19 wherein the cytokine is selected from the following: interferon-.gamma. (INF-.gamma.), interleukin-4 (IL-4), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13) and TGF-.beta..

21. A method of diagnosing a cardiovascular disorder or associated disorder or evaluating whether a subject is susceptible to the disorder, comprising: (a) measuring one or more immunoglobulin levels affected by the disorder to obtain test data; and (b) comparing the test data with reference data to evaluate whether the subject is susceptible to, or has, the cardiovascular disorder or associated disorder.

22. A method according to claim 21 wherein the immunoglobulin is IgG.

23. A method according to claim 22 wherein the IgG is IgG2 subclass.

24. A method according to claim 23 wherein the IgG2 subclass is specific for pathogenic bacteria.

25. A method according to claim 24 wherein the pathogenic bacteria are Chlamydia pneumoniae, Helicobacter pylori or non-typable Haemophilus influenzae.

26. A method according to claim 24 wherein a ratio of total IgG2 to IgG2 subclass specific antibody, or an altered ratio of total IgG2 subclass immunoglobulin to IgG2 subclass specific antibody is an indicator of the presence of or susceptibility to the cardiovascular disorder or associated disorder.

27. A method according to claim 1 wherein the cardiovascular disorder is atheroma, degenerative vascular disease or any cardiovascular condition or disease associated with inflammation of the coronary arteries including 1 to 3 coronary artery disease.

28. A method according to claim 27 wherein the atheroma is atheroma as determined by angiography, with minimal or extensive coronary atherosclerosis but stable clinical disease.

29. A method according to claim 27 wherein the atheroma is part of an unstable clinical disease associated with recent myocardial infarction or unstable angina

30. A method according to claim 1 wherein the cardiovascular associated disorder is hypertension or increased cholesterol levels.

31. Use of an agent for the manufacture of a medicament for the treatment of a cardiovascular disorder or associated disorder wherein said agent is capable of regulating the level or activity of a cytokine associated with the disorder,

32. Use according to claim 31 wherein the cytokine is selected from the group consisting of: interferon-.gamma. (INF-.gamma.), interleukin-4 (IL-4), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13) and TGF-.beta..

33. Use according to claim 31 wherein regulation of the cytokine is achieved by increasing or decreasing the level of the cytokine and/or by potentiating or inhibiting the activity of the cytokine.

34. Use according to claim 33 wherein the regulation of the cytokine is part of a more general switch from a Th2 to a Th1 cytokine profile.

35. Use according to claim 31 wherein the agent is a microorganism, or components, extract or secreted products of a microorganism.

36. Use according to claim 35 wherein the microorganism is yeast or bacteria.

37. Use according to claim 36 wherein the bacteria are probiotic bacteria.

38. Use according to claim 37 wherein the probiotic bacteria are selected from the following: Lactobacillus spp, Mycobacterium spp and Bifidobacterium.

39. Use according to claim 38 wherein the probiotic bacteria are Lactobacillus acidophilus or Mycobacterium vaccae.

40. Use according to claim 35 wherein the microorganism is alive.

41. Use according to claim 31 wherein the agent is an antibody or binding fragment thereof.

42. Use according to claim 31 wherein the cardiovascular disorder or associated disorder is exacerbated by bacterial infection, bacterial antigens, polyclonal activators, super antigens or autoantigens.

43. Use according to claim 42 wherein the cardiovascular disorder or associated disorder is exacerbated by bacterial antigen from Chlamydia pneumoniae, Helicobacterium or non-typable Haemophilus infuenzae.

44. A kit for use in a method according to claim 18

45. A method according to claim 18 wherein the cardiovascular disorder is atheroma, degenerative vascular disease or any cardiovascular condition or disease associated with inflammation of the coronary arteries including 1 to 3 coronary artery disease.

46. A method according to claim 21 wherein the cardiovascular disorder is atheroma, degenerative vascular disease or any cardiovascular condition or disease associated with inflammation of the coronary arteries including 1 to 3 coronary artery disease.

47. A method according to claim 18 wherein the cardiovascular associated disorder is hypertension or increased cholesterol levels.

48. A method according to claim 21 wherein the cardiovascular associated disorder is hypertension or increased cholesterol levels.

49. A kit for use in a method according to claim 21.

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(54) METHODS FOR MONITORING TREATMENT OF HELICOBACTER INFECTION AND FOR PREDICTING THE LIKELIHOOD OF SUCCESSFUL ERADICATION

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(57) ABSTRACT

The present invention relates to methods for monitoring treatment of Helicobacter infection and in particular to methods for monitoring eradication of *Helicobacter pylori* infection using immunoglobulin G2 (IgG2). The invention also relates to methods for predicting the likelihood of successful eradication of Helicobacter infection in a subject to be treated or being treated for the infection and in particular, to methods for predicting the likelihood of successful eradication including determining the levels of interleukin, interferon-γ and IgG in the subject to be, or being treated.

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TITLE: Methods for monitoring treatment of helicobacter infection and for predicting the likelihood of successful eradication

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CLAIMS:

The claims defining the invention are as follows:

1. A method of monitoring eradication of Helicobacter infection in a subject treated for the infection, including: i) determination of IgG2 anti-H. pylori antibody level in a saliva sample; ii) comparison of the IgG2 anti-H. pylori antibody level with a predetermined control IgG2 anti-H. pylori antibody level, wherein a reduction in the level of IgG2 anti-H. pylori antibody in the saliva sample compared to the control indicates eradication of Helicobacter.

2. A method of monitoring efficacy of treatment of Helicobacter infection in a subject treated for the infection, including: i) determination of IgG2 anti-H. pylori antibody level in a saliva sample; ii) comparison of the IgG2 anti-H. pylori antibody level with a predetermined control IgG2 anti-H. pylori antibody level, wherein a reduction in the level of IgG2 anti-H. pylori antibody in the saliva sample compared to the control indicates efficacious treatment of Helicobacter.

3. A method of monitoring relapse or reinfection with Helicobacter in a subject treated for infection with Helicobacter, including: i) determination of IgG2 anti-H. pylori antibody level in a saliva sample; ii) comparison of the IgG2 anti-H. pylori antibody level with a predetermined control IgG2 anti-H. pylori antibody level, wherein an increase in the level of IgG2 anti-H. pylori antibody in the saliva sample compared to the control indicates relapse or reinfection with Helicobacter.

4. A method of detecting unresponsiveness of a subject to treatment of Helicobacter infection, including: (i) determination of IgG2 anti-H. pylori antibody level in a saliva sample; (ii) comparison of the IgG2 anti-H. pylori antibody level with a

predetermined control IgG2 anti-H. pylori antibody level, wherein lack of change in the level of IgG2 anti-H. pylori antibody in the saliva sample compared to the control indicates lack of response to treatment.

5. A method according to any one of claims 1 to 4, wherein the IgG2 anti-H. pylori antibody is detected by an immunoassay.

6. A method according to claim 5, wherein the assay is ELISA.

7. A method according to any one of claims 1 to 6, wherein the control levels of IgG2 anti-H. pylori antibody is established in samples of saliva obtained from subjects not infected by H. pylori.

8. A method according to any one of claims 1 to 6, wherein the control levels of IgG2 anti-H. pylori antibody are determined in subject's own saliva sample.

9. A kit for monitoring treatment of Helicobacter infection, including, (i) Helicobacter antigen (ii) reagent for determining IgG2 subclass antibody.

10. A method of predicting the likelihood of successful eradication of Helicobacter infection in a subject to be treated or being treated for the infection, including: (i) determination of IL-4 level in a sample from the subject; (ii) comparison of the IL-4 level with a predetermined control or standard IL-4 level, (iii) wherein a level of IL-4 in the sample from the subject above the control or standard IL-4 level is predictive of the likelihood of successful eradication and a level of IL-4 below the control or standard IL-4 level is predictive of the likelihood of eradication failure.

11. A method according to claim 10 wherein the sample is a blood sample.

12. A method according to claim 10 or claim 11, wherein the IL-4 is detected by an immunoassay.

13. A method according to claim 12, wherein the assay is ELISA.

14. A method according to any one of claims 10 to 13, wherein the control or standard level of IL-4 is established from analysis of samples obtained from subjects not infected by H. pylori and/or subjects having successfully eradicated H. pylori and/or subjects infected by H. pylori.

15. A method of predicting the likelihood of successful eradication of Helicobacter infection in a subject to be treated or being treated for the infection, including: (i) determination of interferon-.gamma. (INF-.gamma.) level in a sample from the subject; (ii) comparison of the INF-.gamma. level with a predetermined control or standard INF-.gamma. level, (iii) wherein a level of INF-.gamma. in the sample from the subject below the control or standard INF-.gamma. level is predictive of the likelihood of successful eradication and a level of INF-.gamma. above the control or standard level is predictive of the likelihood of eradication failure.

16. A method according to claim 15 wherein the sample is a blood sample.

17. A method according to claim 15 or claim 16, wherein the IFN-.gamma. level is detected by an immunoassay.

18. A method according to claim 17, wherein the assay is ELISA.

19. A method according to any one of claims 15 to 18, wherein the control or standard level of IFN-.gamma. is established from analysis of samples obtained from subjects not infected by H. pylorii and/or subjects having successfully eradicated H. pylori. and/or subjects infected by H. pylori.

20. A method of predicting the likelihood of successful eradication of Helicobacter infection in a subject to be treated or being treated for the infection, including: (i) determination of immunoglobulin G (IgG) level in a sample from the subject; (ii) comparison of the IgG level with a predetermined control or standard IgG level, (iii) wherein a level of IgG in the sample from the subject below the control or standard level is predictive of the likelihood of successful eradication and a level of IgG above the control or standard level is predictive of the likelihood of eradication failure.

21. A method according to claim 20 wherein the sample is a serum sample.

22. A method according to claim 20 wherein the sample is a saliva sample.

23. A method according to any one of claims 20 to 22, wherein the control or standard level of IgG is established from analysis of samples obtained from subjects not infected by H. pylori and/or subjects having successfully eradicated H. pylori and/or subjects infected by H. pylori.

24. A method of predicting the likelihood of successful eradication of Helicobacter infection in a subject to be treated or being treated for the infection, including: (i) determination a combination of IL-4 and/or INF-.gamma. and/or IgG levels in a sample from the subject; (ii) comparison of the IL-4 and/or INF-.gamma. and/or IgG levels with a predetermined control or standard L-4 and/or IF-.gamma. and/or IgG level respectively, wherein a level of IL-4 in the sample from the subject above the control or standard level is predictive of the likelihood of successful eradication and a level of IL-4 below the control or standard level is predictive of the likelihood of eradication failure, and wherein a level of INF-.gamma. in the sample from the subject below the control or standard level is predictive of the likelihood of successful eradication and a level of IFN-.gamma. above the control or standard level is predictive of the likelihood of eradication failure, and wherein a level of IgG in the sample from the subject below the control or standard level is predictive of the likelihood of successful eradication and a level of IgG above the control or standard level is predictive of the likelihood of eradication failure.

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Calenoff

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[54] METHODS AND COMPOSITIONS FOR THE DETECTION AND TREATMENT OF DISEASES ASSOCIATED WITH ANTIGENS OF MICROORGANISMS

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[52] U.S. Cl. 435/7.32; 435/7.33; 435/822; 435/883; 435/975; 436/513; 436/518

[58] Field of Search 435/7.1, 7.2, 7.32, 435/7.33, 259, 883, 961, 962, 822, 41, 69.3, 975; 436/513, 518, 175, 825; 530/416

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[57] ABSTRACT

A library of isolated and purified antigens specific for a microorganism is a set of individual molecules. The library forms antigen-antibody complexes useful in the context of diagnosing and treating conditions associated with a specific microorganism such as *H. pylori*-induced gastro-duodenal disease. For the antigen-antibody complexes in question the antibody is an immunoglobulin, which is IgE if the antigens are allergens. Complexes with IgA, IgG and IgM are also useful. By this multivariate approach, a specific condition is diagnosed with high sensitivity and specificity by determining whether complexes form between a specific antigen library and a biological sample which contains immunoglobulins from an individual. Such libraries also are useful for immunotherapy.

15 Claims, 5 Drawing Sheets

Add 2.0 ml of labeled secondary antibody solution to each strip (2.4x106 CPM/strip). Incubate under gentle agitation at room temperature for 20 hrs.

Wash strips 6 times each as described in 3-a.

Dry the strips at room temp.

Use Fuji BAS 2000 imaging system (Fuji Medical Systems, Stamford, Conn.) to analyze each strip. Determine individual qualitative and quantitative protein band IgE-reactivity

A Modified RAST Test

Generally, in the RAST test an allergen extract is coupled to cellulose particles or paper discs. A patient's serum containing IgE antibody or a control serum is reacted with the allergen-coupled immunosorbent. After thorough washing, labeled antibody is reacted with the immunosorbent. After further washing, the label on the separated sorbent is determined and is a measure of the amount of specific serum IgE antibodies to that allergen.

In an embodiment, the PAST test is modified to increase its sensitivity by removing IgG and/or IgA antibodies which may interfere with IgE binding to the allergen. This is particularly helpful when measuring serum IgE specific to *H. pylori* allergens that are not purified according to the SDS-acetone method of the present invention. Reactants capable of removing IgG, IgM and/or IgA are known in the art, and include, for example, Protein G, anti-human IgG and anti-human IgA, as well as Protein A. For convenience, these reactants are affixed to a solid substrate, including, for example, Sepharose. The amount of the reactants used is sufficient to remove interfering IgG and IgA, but not the IgE which is to be detected. The determination of the desired amount is by methods known to those of skill in the art.

A method of removing interfering IgG and/or IgA antibodies by incubation of the serum with Protein A is discussed in the Examples, infra. Generally, the amount of Protein A which is used is sufficient to prevent the blocking antibodies from competing with the IgE having the same specificity.

The modified RAST test also includes the use of purified protein allergens. Methods of purifying proteins are known in the art and include, for example, differential extraction, salt fractionation, chromatography on ion exchange resins, affinity chromatography and centrifugation. See, for example, Cooper (1977) and Hancock (1984). If antigens are purified by the SDS-acetone method of the present invention "scrubbing" is not needed.

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What is claimed is:

1. A method of detecting in an individual a condition associated with a microorganism, said microorganism selected from the group consisting of a bacterium, a virus, and a mycoplasma, said method comprising:

a. obtaining a library of purified and isolated antigens from a single species of microorganism wherein said library is specific for the condition;

b. measuring an antigen/antibody reaction between (i) immunoglobulin E in a biological sample from the individual, wherein immunoglobulin E is the antibody, and (ii) the isolated antigens of a library of purified antigens specific for the microorganism, and

c. determining whether the condition is present, wherein the presence of said antigen/antibody reaction for said antigens indicates the presence of said condition in the individual.

2. The method of claim **1**, wherein the microorganism is a bacterium.

3. The method of claim **2**, wherein the condition is peptic ulcer disease and the bacterium is *Helicobacter pylori.*

4. The method of claim **2**, wherein the condition is gastritis and the bacterium is *Helicobacter pylori.*

5. The method of claim **2**, wherein the condition is gastric cancer and the bacterium is *Helicobacter pylori.*

6. The method of claim **2**, wherein the condition is nasal polyposis and the bacterium is *Staphyloccus aureus.*

7. The method of claim **2**, wherein the condition is hyperplastic sinusitis and the bacterium is *Staphylococcus aureus.*

8. The method of claim **1**, wherein the antigens are isolated by a process comprising the steps of (i) solubilizing an extract of said microorganism in increasing concentrations of SDS to form fractions and (ii) subfractionating each solubilized fraction by precipitation in increasing concentrations of acetone; and (iii) selecting isolated antigens having a homogeneous molecular weight that are observed as single bands on SDS-PAGE.

9. A method of measuring in a biological sample immunoglobulin E which complexes with a bacterial antigen library, the method comprising:

(a) reacting the sample with a bacterial antigenic library coupled to a solid support, wherein said library consists of isolated and purified antigens from the same bacterial species, and wherein each antigen in the library has a homogeneous molecular weight;

(b) washing and reacting the support with labelled anti-immunoglobulin E; and

(c) detecting the labeled anti-immunoglobulin E bound to the solid support.

10. A method of determining whether an individual has an immunological response to a library of bacterial antigens, said library comprising purified and isolated antigens each having a homogenous molecular weight the method comprising:

(a) providing a biological sample from an individual suspected of containing immunoglobulin E directed to antigens of the library;

(b) providing a composition consisting essentially of isolated antigens of the library;

(c) reacting the biological sample of (a) with the composition of (b) under conditions that allow immunological binding between immunoglobulin E and an antigen to which it is directed; and

(d) detecting complexes formed, if any, between immunoglobulin E in the serum of (a) and a protein antigen in the composition of (b) such that the presence of the immunoglobulin is inferred and whether an individual has an immunological response is determined.

11. The method of claim 10, wherein the serum provided has been reacted with a composition capable of removing IgA and IgG from the serum in amount sufficient to remove IgG and IgA which interferes with formation of the IgE-allergen complex.

12. The method of claim 10 wherein the composition of Step b comprises protein allergens of *H. pylori*.

13. A diagnostic kit comprising a library of isolated and purified microbial antigens from the same microorganism each antigen in solution in a suitable container, and means for detecting immunological complexes formed between the library of antigens from the same microorganism and immunoglobulin E in a biological sample.

14. The kit of claim 13, wherein the library is specific for *H. pylori*.

15. The kit of claim 13, wherein the antigens are coupled to a solid support.

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Pang et al. (43) **Pub. Date: Jul. 1, 2004**

(54) **COMPOSITIONS AND METHODS FOR DIAGNOSIS AND TREATMENT OF CARDIOVASCULAR DISORDERS**

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(57) **ABSTRACT**

There is disclosed a method of prophylactic or therapeutic treatment of a cardiovascular disorder comprising administering to a subject in need thereof an effective amount of one or more agents for upregulating a cytokine profile characteristic of a Th1 T-cell response relative to a cytosine profile of a Th2 T-cell response associated with the disorder. There is further disclosed compositions for use in the methods.